REMARKS

Upon entry of the foregoing amendment, claims 2-7, 11, 13, 14, 16, 19, 31, 32, 38 and 46-60 are pending in this application. Claims 1, 8-10, 12, 15, 17, 18, 20-30, 33-37 and 39-45 are canceled without prejudice or disclaimer. New claims 46-60 have been added. Applicants reserve the right to pursue claims directed to the canceled subject matter in a continuing or divisional application. Claims 2-7, 11, 13, 14, 16, 19, 31, 32, 38 and 46-60 are currently under examination.

Support for the amendments to claim 2 is found as follows:

for the phrase "at least one" is found, for example, in original claims 8, 11-13; on page 10, lines 24-25; and, elsewhere throughout the specification;

for the phrase "formulation" is found, for example, in original claim 2; and, elsewhere throughout the specification;

for the phrase " is applied in dry form" is found, for example, on page 8, lines 6-8; Examples 1-3; and, elsewhere throughout the specification;

for the phrase "in an amount and for a length of time effective to induce an immune response" is found, for example on page 12, lines 32-33; page 21, lines 32-33; original claim 38; and, elsewhere throughout the specification.

Support for the amendments to claim 7 for "bacterial DNA, chemokines, tumor necrosis factor alpha, genetically altered toxins, chemically conjugated bacterial ADP ribosylating exotoxins" is found, for example, on page 20, line 4 through page 23, line 27; and, elsewhere throughout the specification.

Support for the amendments to claim 38 is found, for example, in original claims 1 and 2, and, elsewhere throughout the specification.

Support for new claims 46, 47, 59 and 60 is found, for example, in original claim 11; on page 19, lines 4-11 and 12-21; and, elsewhere throughout the specification.

Support for new claims 48, 49, 54 and 55 is found, for example, on pages 42-44 (Example 4); and elsewhere throughout the specification.

Support for new claims 50 and 57 is found, for example, on pages 44-54 (Examples 5-7); and, elsewhere throughout the specification.

Support for new claims 51 and 53 is found, for example, on pages 42-47 (Examples 4 and 5); and, elsewhere throughout the specification.

Support for new claim 52 is found, for example, in original claim 3; and, elsewhere throughout the specification.

Support for new claim 56 is found, for example, in original claim 19; and, elsewhere throughout the specification.

Support for new claim 58 is found, for example, in original claim 11; and, elsewhere throughout the specification.

No new matter is believed to have been added. In view of the amendments and following remarks, reconsideration of the rejections and withdrawal thereof is respectfully requested. This amendment is in response to the Final Office Action, dated August 6, 2002 in parent application no. 09/545,417.

Interviews

Applicants appreciate the Examiner's efforts in furthering the prosecution of this Application by granting an interview on August 7, 2003. Applicants' representative and the Examiner discussed streamlining the pending applications to find allowable subject matter and suggested amendments to the claims to overcome outstanding rejections. The comments made by the Examiner have been considered when preparing this response and the Examiner's suggested claim amendments are believed to be incorporated in the claims as currently amended. In view of the discussion during the interview, the above amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and timely allowance of the pending claims.

Rejection under 35 USC § 112, first paragraph

The Office rejected claims 2-7, 10, 11, 13-16 and 19-39 under 35 USC §112, first paragraph, because the specification, while being enabling for, in particular, "a method of inducing an immune response comprising applying a formulation to intact skin where said formulation comprises a pathogenic antigen which a cholera toxin (CT) or LT adjuvant, wherein said formulation is in dry form" does not reasonably provide enablement for other embodiments as claimed. Applicants respectfully traverse the rejection.

Without acquiescing to Office arguments, Applicants have canceled claims 10, 15, 20-30, 33-37 and 39, directed to subject matter alleged by the Office to lack enablement. Applicants have amended claim 2 to include the phrase "applied in dry form" in view of remarks made at page 4 of the Office Action, where the Examiner argues the limitation is an unclaimed limitation. This amendment to the claim is believed to overcome part A of the rejection (Office Action, page 2).

Applicants have canceled the claims directed to methods involving activating Langerhans cells

(part B); to methods directed to increasing major histocompatibility complex class II expression (part C); to methods involving migration of underlying Langerhans cells (part D); to methods involving signalling underlying Langerhans cells (part E); to methods involving enhancing antigen presentation (part F); and, to methods involving an immune response comprised of an antigen specific lymphocyte (part G). Applicants direct the attention of the Examiner to U.S. Patent No. 5,910,306 and 5,980,898 and the subject matter of the issued claims therein. Applicants reserve the right to pursue claims directed to the same or similar subject matter of the canceled claims in a continuing or divisional application.

Regarding the rejection of claim 14, directed to live attenuated viruses, the Office has previously (Office Action dated 12/04/01) argued that the "claim essentially means that the skin provides no protection to viruses at all (as said virus would pass through the skin) and that a subject would become infected or immunized to all viruses in which said subject comes in contact. It is well known that in the immunological arts that subjects are neither immunized nor infected after skin contact with most viruses, e.g., HIV. Thus, the invention as broadly claimed, must be considered highly unpredictable; said invention would required undue experimentation to practice as claimed" and has maintained the rejection to date.

Applicants disagree with the Office's interpretation of claim 14. In making and retaining this rejection, the Office has not considered the claim in its entirety. The language of the rejection indicates the Office has interpreted claim 14 to use a virus alone, and not in conjunction with an adjuvant as is claimed. Claim 14 is now, and was then, directed to a method of inducing an immune response comprising applying a formulation comprising, *inter alia*, an adjuvant and an attenuated live virus wherein the antigen is expressed by the virus. The method as claimed requires the use of an adjuvant in combination with the virus and does not claim the use of the virus alone. Thus, the argument which is the basis of the rejection is not commensurate with the scope of the claim.

The Office argues that Gupta *et al.* was cited for its teaching that adjuvants are unpredictable, i.e., that adjuvants are not interchangeable ("Several adjuvants act with certain specific antigens and are not effective with other antigens," citing Gupta *et al.*) and that the WO 98/2074 and U.S. Appl. No. 09/257,188 teach the same closely related adjuvants as the instant specification.

However, contrary to the position of the Office regarding the unpredictability of antigen-adjuvant combinations, the specification is enabling for the broad scope of claim 2 (as currently amended) regarding adjuvants. The claims should not be limited to one or even to a group of closely related adjuvants. It is well settled that even if some of the antigen-adjuvant combinations are inoperative, the claims are not necessarily invalid. It is not a function of the claims to specifically exclude possible inoperative substances. Even if the claim were to include, for the sake of argument, possible inoperative embodiments, the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. (MPEP, § 2164.08(b), Eighth edition, August 2001, revised February 2003, citing *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984)). A disclosure of a large number of operable embodiments and the identification of a single inoperative embodiment does not render a claim broader than the enabled scope because undue experimentation was not involved in determining those embodiments that were operable. (MPEP, § 2164.08(b), Eighth edition, August 2001, revised February 2003, citing *In re Angstadt*, 537 F.2d 498, 502-503, 190 USPQ 214, 218 (CCPA 1976)).

At pages 19-24, the specification describes a wide variety of adjuvants useful in the practice of the invention. At pages 17-19, the specification describes a wide variety of antigens useful in the practice of the invention. At pages 37-55, the specification describes a large number of operative embodiments. Applicants assert that a skilled person could determine which antigen-adjuvant

combinations would be inoperative or operative without undue experimentation using procedures detailed in the instant specification. See, specification pages 33-36, describing ELISA procedures for detecting IgG, IgM and IgA antibodies produced in response to **any** antigen-adjuvant combination.

Contrary to the arguments of the Office, the specification teaches one of skill in the art how to determine which antigen-adjuvant combinations are operative or inoperative without undue experimentation. Further, the teachings of Gupta *et al.,* relied on for describing the lack of adjuvant interchangeability, do not override still valid case law holdings that the possible existence of some inoperative embodiments fail to render a claim non-enabled. Reconsideration and withdrawal of the rejection is respectfully requested.

The Office statement, page 4, bottom, that "Applicants' assertion that 'The weight of evidence in support of the enabling nature of the disclosure of the specification is firmly in favor of the conclusion that undue experimentation would not be needed to practice the present invention and that the enablement rejections are not support by any factual evidence' is simply legally and scientifically incorrect" is itself incorrect. It is well settled (see, above) that claims do not lack enablement simply because the scope possibly includes some inoperative embodiments.

The rejection of claims 2-7, 11, 13, 14, 16 and 19, 31, 32 and 38, and claims dependent therefrom, under 35 USC § 112, first paragraph, is believed to be overcome in view of the amendments to the claims and arguments above. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 33-35 under 35 USC § 112, second paragraph

Claims 33-35 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. Applicants respectfully traverse the rejection.

In reply thereto, and without acquiescing to either the arguments or the position of the Office, claims 33-35 have been canceled. The rejection is therefore moot. Applicants reserve the right to pursue the subject matter of claims 33-35 in a continuing or divisional application. Withdrawal of the rejection is respectfully requested.

Provisional Rejection under 35 USC § 103(a)

Claims 2, 6, 10, 11, 13, 15, 16, 19-22, 28-30, 32 and 38 stand provisionally rejected under 35 USC §103(a) as being obvious over copending application no. 09/337,746. Applicants respectfully traverse the rejection. Claims 10, 15, 20-22 and 28-30 have been canceled.

The Office asserts the inclusion of "dry" in the instant claims does not render them patentably distinct from the claims of the '746 application; that the instant claims are considered broader than the claims of the '746 application and therefore the '746 application renders the claims of the instant application obvious, but not vice versa.

The '746 application is assigned to the Government of the United States. The instant application is assigned to Iomai Corporation. The inventions were not commonly owned at the time the different inventive entities made their inventions.

Applicants assert the '746 application is not proper prior art against the instant claims. Contrary to the arguments of the Office, the '746 application does <u>not</u> claim priority to Appl. No. 60/128,370, filed April 8, 1999. A substitute declaration was filed with the PTO on October 10, 2001, dropping the priority claim to 60/128,370. A copy of the substitute declaration is provided herein as Exhibit A. A copy of the PTO date-stamped paper showing receipt of both the substitute declaration and new assignment is attached as Exhibit B. A copy of the Official Filing

Receipt, dated 2/26/02, showing no priority claim to Appl. No. 60/128,370 is attached as Exhibit C.

The '746 application no longer claims priority to the 60/128,370 application and therefore loses the benefit of the April 8, 1999 priority date. After the loss of priority to April 8, 1999, the '746 application no longer has an earlier filing date than the instant application and cannot be applied as prior art. If the Office maintains this rejection over the '746 application by way of priority claims to other applications, the Office is respectfully requested to meet its burden and point out with particularity (line, paragraph, claim, etc.) support for a method comprising a dry formulation in the priority application/patent so that Applicants may address and resolve any outstanding issues.

The rejection over the '746 copending application has been overcome by withdrawal of the priority claim to the 60/128,370 application. Reconsideration and withdrawal of the rejection is believed to be appropriate and is respectfully requested.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and timely allowance of the pending claims. A favorable action is awaited. Should the Examiner believe an interview would be helpful to further allowance of this application, the Examiner is invited to telephone the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. § 1.16 and § 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph

is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. § 1.136(a)(3).

Exhibits A-C:

A: copy of substitute declaration filed Oct. 10, 2001

B: copy of PTO date stamped paper showing receipt of substitute declaration

C: copy of the Official Filing Receipt, mail dated 2/26/02

Date: November 5, 2003

Respectfully submitted,
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